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     (FILE 'HOME' ENTERED AT 18:08:39 ON 02 DEC 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:08:51 ON 02 DEC
     2003
L1          105 S E4ORF4
L2            5 S (DNA OR POLYNUCLEOTIDE OR CDNA OR NUCLEOTIDE OR NUCLEIC(W)ACI
L3            2 DUP REM L2 (3 DUPLICATES REMOVED)
L4           45 DUP REM L1 (60 DUPLICATES REMOVED)

=> d bib ab 1-2 l3

L3   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   1998:66000  CAPLUS
DN   128:136504
TI   Use of adenovirus E4 death proteins to induce p53-independent apoptosis
IN   Branton, Philip E.; Shore, Gordon C.; Teodoro, Jose G.; Marcellus, Richard
     C.; Lavoie, Josee N.
PA   Branton, Philip E., Can.; Shore, Gordon C.; Teodoro, Jose G.; Marcellus,
     Richard C.; Lavoie, Josee N.
SO   PCT Int. Appl., 88 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9801563         A2   19980115       WO 1997-IB1041   19970703
         W:  AU, CA, JP, US, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     CA 2259152         AA   19980115       CA 1997-2259152  19970703
     CA 2259152         C    20020212
     AU 9738601         A1   19980202       AU 1997-38601    19970703
     AU 731924          B2   20010405
     EP 951553          A2   19991027       EP 1997-935709   19970703
     EP 951553          B1   20031029
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2000515504      T2   20001121       JP 1998-504995   19970703
PRAI US 1996-21273P     P    19960705
     US 1996-28740P     P    19961022
     WO 1997-IB1041     W    19970703
AB   A method for therapeutic induction of p53-independent apoptosis using the
     adenovirus E4 death proteins E4orf4 or E4orf6 or the genes for these
     proteins is described.  Biol. active fragments of the proteins, or analogs
     of the proteins may also be used.  Methods for identifying analogs and
     mimetics of the adenovirus E4 death proteins are also discussed.  These
     proteins induce apoptosis in the absence of the E1A and E1B gene products.

L3   ANSWER 2 OF 2     MEDLINE on STN                    DUPLICATE 1
AN   92407980      MEDLINE
DN   92407980    PubMed ID: 1326648
TI   Adenovirus E4orf4 protein reduces phosphorylation of c-Fos and E1A
     proteins while simultaneously reducing the level of AP-1.
AU   Muller U; Kleinberger T; Shenk T
CS   Department of Molecular Biology, Howard Hughes Medical Institute,
     Princeton University, New Jersey 08544-1014.
NC   CA38965 (NCI)
SO   JOURNAL OF VIROLOGY, (1992 Oct) 66 (10) 5867-78.
     Journal code: 0113724. ISSN: 0022-538X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
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LA English
FS Priority Journals
EM 199210
ED Entered STN: 19921106
Last Updated on STN: 19921106
Entered Medline: 19921019
AB Adenovirus E1A protein and cyclic AMP cooperate to induce transcription factor AP-1 and viral gene expression in mouse S49 cells. We report that a protein encoded within the viral E4 gene region acts to counterbalance the induction of AP-1 DNA-binding activity by E1A and cyclic AMP. Studies with mutant adenoviruses demonstrated that in the absence of **E4orf4** protein, AP-1 **DNA**-binding activity is induced to substantially higher levels than in wild-type virus-infected cells. The induction is the result of increased production of JunB and c-Fos proteins. Hyperphosphorylated forms of c-Fos and E1A proteins accumulate in the absence of functional E4orf4 protein. We propose that the E4orf4 protein acts to inhibit the activity of a cellular kinase that phosphorylates both the E1A and c-Fos proteins. Phosphorylation-dependent alterations in the activity of c-Fos, E1A, or some unidentified protein might, then, lead to decreased synthesis of AP-1 components. This E4 function likely plays an important role in natural infections, since a mutant virus unable to express the E4orf4 protein is considerably more cytotoxic than the wild-type virus.

=> d au ti so 1-45 l4

L4 ANSWER 1 OF 45 MEDLINE on STN
AU Rexroad Jason; Wiethoff Christopher M; Green Anthony P; Kierstead Timothy D; Scott Miller O; Middaugh C Russell
TI Structural stability of adenovirus type 5.
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (2003 Mar) 92 (3) 665-78.
Journal code: 2985195R. ISSN: 0022-3549.

L4 ANSWER 2 OF 45 MEDLINE on STN
AU Doronin Konstantin; Toth Karoly; Kuppuswamy Mohan; Krajcsi Peter; Tollefson Ann E; Wold William S M
TI Overexpression of the ADP (E3-11.6K) protein increases cell lysis and spread of adenovirus.
SO VIROLOGY, (2003 Jan 20) 305 (2) 378-87.
Journal code: 0110674. ISSN: 0042-6822.

L4 ANSWER 3 OF 45 MEDLINE on STN DUPLICATE 1
AU Van Hoof Christine; Goris Jozef
TI Phosphatases in apoptosis: to be or not to be, PP2A is in the heart of the question.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (2003 May 12) 1640 (2-3) 97-104. Ref: 53
Journal code: 0217513. ISSN: 0006-3002.

L4 ANSWER 4 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Kaplan, Johanne [Inventor, Reprint Author]; Armentano, Donna [Inventor]; Gregory, Richard J. [Inventor]
TI Transgene expression systems.
SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 26, 2002) Vol. 1264, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).

L4 ANSWER 5 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Strack S (Reprint); Ruediger R; Walter G; Dagda R K; Barwacz C A; Cribbs J T
TI Protein phosphatase 2A holoenzyme assembly - Identification of contacts between B-family regulatory and scaffolding a subunits
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (7 JUN 2002) Vol. 277, No. 23, pp.

20750-20755.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.

L4 ANSWER 6 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Silverstein A M; Barrow C A; Davis A J; Mumby M C (Reprint)
TI Actions of PP2A on the MAP kinase pathway and apoptosis are mediated by distinct regulatory subunits
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2 APR 2002) Vol. 99, No. 7, pp. 4221-4226.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.

L4 ANSWER 7 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Hay S; Kannourakis G (Reprint)
TI A time to kill: viral manipulation of the cell death program
SO JOURNAL OF GENERAL VIROLOGY, (JUL 2002) Vol. 83, Part 7, pp. 1547-1564.
Publisher: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AE, BERKS, ENGLAND.
ISSN: 0022-1317.

L4 ANSWER 8 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU McCluskey A (Reprint); Sim A T R; Sakoff J A
TI Serine-threonine protein phosphatase inhibitors: Development of potential therapeutic strategies
SO JOURNAL OF MEDICINAL CHEMISTRY, (14 MAR 2002) Vol. 45, No. 6, pp. 1151-1175.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0022-2623.

L4 ANSWER 9 OF 45 MEDLINE on STN DUPLICATE 2
AU Robert Amelie; Miron Marie-Joelle; Champagne Claudia; Gingras Marie-Claude; Branton Philip E; Lavoie Josee N
TI Distinct cell death pathways triggered by the adenovirus early region 4 ORF 4 protein.
SO JOURNAL OF CELL BIOLOGY, (2002 Aug 5) 158 (3) 519-28.
Journal code: 0375356. ISSN: 0021-9525.

L4 ANSWER 10 OF 45 MEDLINE on STN
AU Katabi Maha; Yuan Shala; Chan Helen; Galipeau Jacques; Batist Gerald
TI The nonapoptotic pathway mediating thymidine kinase/ganciclovir toxicity is reduced by signal from adenovirus type 5 early region 4.
SO MOLECULAR THERAPY, (2002 Feb) 5 (2) 170-6.
Journal code: 100890581. ISSN: 1525-0016.

L4 ANSWER 11 OF 45 MEDLINE on STN DUPLICATE 3
AU Gingras Marie-Claude; Champagne Claudia; Roy Melanie; Lavoie Josee N
TI Cytoplasmic death signal triggered by SRC-mediated phosphorylation of the adenovirus **E4orf4** protein.
SO MOLECULAR AND CELLULAR BIOLOGY, (2002 Jan) 22 (1) 41-56.
Journal code: 8109087. ISSN: 0270-7306.

L4 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2003 ACS on STN
IN Branton, Philip E.; Marcellus, Richard C.; Shore, Gordon C.; Roopchand, Diana E.; Lee, Joseph M.; Shahinian, S. Serge; Bussey, A. Howard
TI **E4orf4** and PP2A polypeptides, modulators, and mimetics for selectively inducing cell death
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2

L4 ANSWER 13 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Gjoerup O; Zaveri D; Roberts T M (Reprint)

TI Induction of p53-independent apoptosis by simian virus 40 small t antigen
SO JOURNAL OF VIROLOGY, (OCT 2001) Vol. 75, No. 19, pp. 9142-9155.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0022-538X.

L4 ANSWER 14 OF 45 MEDLINE on STN DUPLICATE 4
AU Branton P E; Roopchand D E
TI The role of adenovirus **E4orf4** protein in viral replication and cell killing.
SO ONCOGENE, (2001 Nov 26) 20 (54) 7855-65. Ref: 99
Journal code: 8711562. ISSN: 0950-9232.

L4 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2003 ACS on STN
AU Afifi, Rana; Sharf, Rakefet; Shtrichman, Ronit; Kleinberger, Tamar
TI Selection of apoptosis-deficient adenovirus **E4orf4** mutants in Saccharomyces cerevisiae. [Erratum to document cited in CA135:43435]
SO Journal of Virology (2001), 75(12), 5719
CODEN: JOVIAM; ISSN: 0022-538X

L4 ANSWER 16 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Afifi R (Reprint); Sharf R; Shtrichman R; Kleinberger T
TI Selection of apoptosis-deficient adenovirus **e4orf4** mutants in Saccharomyces cerevisiae (vol 75, pg 4444, 2001)
SO JOURNAL OF VIROLOGY, (JUN 2001) Vol. 75, No. 12, pp. 5719-5719.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0022-538X.

L4 ANSWER 17 OF 45 MEDLINE on STN DUPLICATE 5
AU Roopchand D E; Lee J M; Shahinian S; Paquette D; Bussey H; Branton P E
TI Toxicity of human adenovirus **E4orf4** protein in Saccharomyces cerevisiae results from interactions with the Cdc55 regulatory B subunit of PP2A.
SO ONCOGENE, (2001 Aug 30) 20 (38) 5279-90.
Journal code: 8711562. ISSN: 0950-9232.

L4 ANSWER 18 OF 45 MEDLINE on STN DUPLICATE 6
AU Afifi R; Sharf R; Shtrichman R; Kleinberger T
TI Selection of apoptosis-deficient adenovirus **E4orf4** mutants in Saccharomyces cerevisiae.
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Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 19 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Marcellus R C (Reprint); Chan H L; Paquette D; Zhang Z; Szymborski A; Miron M; Lavoie J N; Pallas D C; Shore G C; Branton P E
TI Adenovirus **E4orf4** specifically kills cancer lines via an interaction with PP2A.
SO CLINICAL CANCER RESEARCH, (NOV 2001) Vol. 7, No. 11, Supp. [S], pp. 3715S-3715S. MA 303.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
ISSN: 1078-0432.

L4 ANSWER 20 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Ruediger R; Pham H T; Walter G (Reprint)
TI Alterations in protein phosphatase 2A subunit interaction in human carcinomas of the lung and colon with mutations in the A beta subunit gene
SO ONCOGENE, (5 APR 2001) Vol. 20, No. 15, pp. 1892-1899.
Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 0950-9232.

L4 ANSWER 21 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Nilsson C E; Petersen-Mahrt S; Durot C; Shtrichman R; Krainer A R; Kleinberger T; Akusjarvi G (Reprint)
TI The adenovirus E4-ORF4 splicing enhancer protein interacts with a subset of phosphorylated SR proteins
SO EMBO JOURNAL, (15 FEB 2001) Vol. 20, No. 4, pp. 864-871.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.

L4 ANSWER 22 OF 45 MEDLINE on STN DUPLICATE 7
AU Livne A; Shtrichman R; Kleinberger T
TI Caspase activation by adenovirus **e4orf4** protein is cell line specific and Is mediated by the death receptor pathway.
SO JOURNAL OF VIROLOGY, (2001 Jan) 75 (2) 789-98.
Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 23 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Janssens V; Goris J (Reprint)
TI Protein phosphatase 2A: a highly regulated family of serine/threonine phosphatases implicated in cell growth and signalling
SO BIOCHEMICAL JOURNAL, (1 FEB 2001) Vol. 353, Part 3, pp. 417-439.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND.
ISSN: 0264-6021.

L4 ANSWER 24 OF 45 MEDLINE on STN DUPLICATE 8
AU Kornitzer D; Sharf R; Kleinberger T
TI Adenovirus **E4orf4** protein induces PP2A-dependent growth arrest in Saccharomyces cerevisiae and interacts with the anaphase-promoting complex/cyclosome.
SO JOURNAL OF CELL BIOLOGY, (2001 Jul 23) 154 (2) 331-44.
Journal code: 0375356. ISSN: 0021-9525.

L4 ANSWER 25 OF 45 MEDLINE on STN
AU Baxi M K; Robertson J; Babiuk L A; Tikoo S K
TI Mutational analysis of early region 4 of bovine adenovirus type 3.
SO VIROLOGY, (2001 Nov 10) 290 (1) 153-63.
Journal code: 0110674. ISSN: 0042-6822.

L4 ANSWER 26 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Sontag E (Reprint)
TI Protein phosphatase 2A: the Trojan Horse of cellular signaling
SO CELLULAR SIGNALLING, (JAN 2001) Vol. 13, No. 1, pp. 7-16.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010 USA.
ISSN: 0898-6568.

L4 ANSWER 27 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Kaplan, Johanne [Inventor, Reprint author]; Armentano, Donna [Inventor]; Gregory, Richard J. [Inventor]
TI Transgene expression systems.
SO Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 8, 2000) Vol. 1237, No. 2. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.

L4 ANSWER 28 OF 45 MEDLINE on STN DUPLICATE 9
AU Marcellus R C; Chan H; Paquette D; Thirlwell S; Boivin D; Branton P E
TI Induction of p53-independent apoptosis by the adenovirus **E4orf4** protein requires binding to the Balpha subunit of protein phosphatase 2A.
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Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 29 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU Hrimech M; Yao X J; Branton P E; Cohen E A (Reprint)
TI Human immunodeficiency virus type 1 Vpr-mediated G(2) cell cycle arrest:

Vpr interferes with cell cycle signaling cascades by interacting with the B subunit of serine/threonine protein phosphatase 2A
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Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.

L4 ANSWER 30 OF 45 MEDLINE on STN DUPLICATE 10
AU Shtrichman R; Sharf R; Kleinberger T
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SO ONCOGENE, (2000 Aug 3) 19 (33) 3757-65.
Journal code: 8711562. ISSN: 0950-9232.

L4 ANSWER 31 OF 45 MEDLINE on STN DUPLICATE 11
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TI Adenovirus E4 open reading frame 4-induced apoptosis involves dysregulation of Src family kinases.
SO JOURNAL OF CELL BIOLOGY, (2000 Sep 4) 150 (5) 1037-56.
Journal code: 0375356. ISSN: 0021-9525.

L4 ANSWER 32 OF 45 MEDLINE on STN DUPLICATE 12
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SO APOPTOSIS, (2000 Jun) 5 (3) 211-5. Ref: 37
Journal code: 9712129. ISSN: 1360-8185.

L4 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2003 ACS on STN
AU Szala, Stanislaw
TI Specific induction of apoptosis in cancer cells
SO Nowotwory (2000), 50(2), 111-121
CODEN: NOWOAL; ISSN: 0029-540X

L4 ANSWER 34 OF 45 MEDLINE on STN DUPLICATE 13
AU Shtrichman R; Sharf R; Barr H; Dobner T; Kleinberger T
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SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Aug 31) 96 (18) 10080-5.
Journal code: 7505876. ISSN: 0027-8424.

L4 ANSWER 35 OF 45 MEDLINE on STN DUPLICATE 14
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L4 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2003 ACS on STN
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TI Adenoviral vectors comprising a modified e4 region but retaining e4orf3
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2

L4 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2003 ACS on STN
IN Branton, Philip E.; Shore, Gordon C.; Teodoro, Jose G.; Marcellus, Richard C.; Lavoie, Josee N.
TI Use of adenovirus E4 death proteins to induce p53-independent apoptosis
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2

L4 ANSWER 38 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AU Hardwick, J. Marie [Reprint author]; Ketner, Gary [Reprint author]; Clem, Rollie J.
TI Viral genes that modulate apoptosis.
SO Wilson, J. W. [Editor]; Booth, C. [Editor]; Potten, C. S. [Editor]. (1998) pp. 243-279. Apoptosis genes. print.
Publisher: Kluwer Academic Publishers, 101 Phillip Drive, Norwell, Massachusetts 02061, USA; Kluwer Academic Publishers, PO Box 989, 3300 AZ Dordrecht, The Netherlands.
ISBN: 0-412-83860-5.

L4 ANSWER 39 OF 45 MEDLINE on STN DUPLICATE 15
AU Marcellus R C; Lavoie J N; Boivin D; Shore G C; Ketner G; Branton P E
TI The early region 4 orf4 protein of human adenovirus type 5 induces p53-independent cell death by apoptosis.
SO JOURNAL OF VIROLOGY, (1998 Sep) 72 (9) 7144-53.
Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 40 OF 45 MEDLINE on STN DUPLICATE 16
AU Shtrichman R; Kleinberger T
TI Adenovirus type 5 E4 open reading frame 4 protein induces apoptosis in transformed cells.
SO JOURNAL OF VIROLOGY, (1998 Apr) 72 (4) 2975-82.
Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 41 OF 45 MEDLINE on STN DUPLICATE 17
AU Lavoie J N; Nguyen M; Marcellus R C; Branton P E; Shore G C
TI **E4orf4**, a novel adenovirus death factor that induces p53-independent apoptosis by a pathway that is not inhibited by zVAD-fmk.
SO JOURNAL OF CELL BIOLOGY, (1998 Feb 9) 140 (3) 637-45.
Journal code: 0375356. ISSN: 0021-9525.

L4 ANSWER 42 OF 45 MEDLINE on STN DUPLICATE 18
AU Whalen S G; Marcellus R C; Whalen A; Ahn N G; Ricciardi R P; Branton P E
TI Phosphorylation within the transactivation domain of adenovirus E1A protein by mitogen-activated protein kinase regulates expression of early region 4.
SO JOURNAL OF VIROLOGY, (1997 May) 71 (5) 3545-53.
Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 43 OF 45 MEDLINE on STN DUPLICATE 19
AU Kleinberger T; Shenk T
TI Adenovirus **E4orf4** protein binds to protein phosphatase 2A, and the complex down regulates E1A-enhanced junB transcription.
SO JOURNAL OF VIROLOGY, (1993 Dec) 67 (12) 7556-60.
Journal code: 0113724. ISSN: 0022-538X.

L4 ANSWER 44 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AU KLEINBERGER T (Reprint); MULLER U; SHENK T
TI ADENOVIRUS-**E4ORF4** PROTEIN ASSOCIATES WITH PHOSPHATASE-2A AND CONTROLS PHOSPHORYLATION AND GENE-EXPRESSION IN ADENOVIRUS-INFECTED CELLS
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L4 ANSWER 45 OF 45 MEDLINE on STN DUPLICATE 20
AU Muller U; Kleinberger T; Shenk T
TI Adenovirus **E4orf4** protein reduces phosphorylation of c-Fos and E1A proteins while simultaneously reducing the level of AP-1.
SO JOURNAL OF VIROLOGY, (1992 Oct) 66 (10) 5867-78.
Journal code: 0113724. ISSN: 0022-538X.

=> d ab 43-45 l4

L4 ANSWER 43 OF 45 MEDLINE on STN DUPLICATE 19

AB Adenovirus **E4orf4** protein was previously shown to counteract transactivation of junB by cyclic AMP (cAMP) and E1A protein. It was also shown to cause hypophosphorylation of E1A and c-Fos proteins. Here we show that the **E4orf4** protein associates with protein phosphatase 2A. All three subunits of the phosphatase are present in the complex, and the B subunit interacts directly with the viral protein. The complex possesses a phosphatase activity typical of protein phosphatase 2A, and the phosphatase mediates the **E4orf4**-induced down regulation of junB transcription. Thus, adenovirus **E4orf4** protein recruits protein phosphatase 2A into a signal transduction pathway initiated by cAMP and E1A protein.

L4 ANSWER 44 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

L4 ANSWER 45 OF 45 MEDLINE on STN DUPLICATE 20

AB Adenovirus E1A protein and cyclic AMP cooperate to induce transcription factor AP-1 and viral gene expression in mouse S49 cells. We report that a protein encoded within the viral E4 gene region acts to counterbalance the induction of AP-1 DNA-binding activity by E1A and cyclic AMP. Studies with mutant adenoviruses demonstrated that in the absence of **E4orf4** protein, AP-1 DNA-binding activity is induced to substantially higher levels than in wild-type virus-infected cells. The induction is the result of increased production of JunB and c-Fos proteins. Hyperphosphorylated forms of c-Fos and E1A proteins accumulate in the absence of functional **E4orf4** protein. We propose that the **E4orf4** protein acts to inhibit the activity of a cellular kinase that phosphorylates both the E1A and c-Fos proteins. Phosphorylation-dependent alterations in the activity of c-Fos, E1A, or some unidentified protein might, then, lead to decreased synthesis of AP-1 components. This E4 function likely plays an important role in natural infections, since a mutant virus unable to express the **E4orf4** protein is considerably more cytotoxic than the wild-type virus.

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